ATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGGCGCGGGAGT
GCTGCCTGCCCACGGCACCCAGCACGGCATCCGGCTGCCCCTGCGCA
GCGGCCTGGGGGGCGCCCCCCTGGGGCTGCGGCTGCCCCGGGAGAC
CGACGAAGAGCCCGAGGAGCCCGGCCGGAGGGGCAGCTTTGTGGAGA
TGGTGGACAACCTGAGGGGCAAGTCGGGGCAGGGCTACTACGTGGAG
ATGACCGTGGGCAGCCCCCCGCAGACGCTCAACATCCTGGTGGATACA
GGCAGCAGTAACTTTGCAGTGGGTGCTGCCCCCCACCCCTTCCTGCAT
330 CGCTACTACCAGAGGCAGCTGTCCAGCACATACCGGGACCTCCGGAAG
GGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAGCTGGG
CACCGACCTGGTAAGCATCCCCCATGGCCCCAACGTCACTGTGCGTGC
CAACATTGCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCC
AACTGGGAAGGCATCCTGGGGCTGGCCTATGCTGAGATTGCCAGGCCT
GACGACTCCCTGGAGCCTTTCTTTGACTCTCTGGTAAAGCAGACCCACG
TTCCCAACCTCTTCTCCCTGCAGCTTTGTGGTGCTGGCTTCCCCCTCAA
CCAGTCTGAAGTGCTGGCCTCTGTCGGAGGGAGCATGATCATTGGAGG
TATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATACACCCATCCGG
CGGGAGTGGTATTATGAGGTGATCATTGTGCGGGTGGAGATCAATGGA
CAGGATCTGAAAATGGACTGCAAGGAGTACAACTATGACAAGAGCATTG
TGGACAGTGGCACCACCAACCTTCGTTTGCCCAAGAAAGTGTTTGAAGC
TGCAGTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGAT
GGTTTCTGGCTAGGAGAGCAGCTGGTGTGCTGGCAAGCAGGCACCACC
CCTTGGAACATTTTCCCAGTCATCTCACTCTACCTAATGGGTGAGGTTAC
CAACCAGTCCTTCCGCATCACCATCCTTCCGCAGCAATACCTGCGGCCA
GTGGAAGATGTGGCCACGTCCCAAGACGACTGTTACAAGTTTGCCATCT
CACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTT
CTACGTTGTCTTTGATCGGGCCCGAAAACGAATTGGCTTTGCTGTCAGC
GCTTGCCATGTGCACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCT
TTTGTCACCTTGGACATGGAAGACTGTGGCTACAACATTCCACAGACAG
ATGAGTCAACCCTCATGACCATAGCCTATGTCATGGCTGCCATCTGCGC
CCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTCAGTGGCGCTGCCTC
CGCTGCCTGCGCCAGCAGCATGATGACTTTGCTGATGACATCTCCCTGC
TGAAG

FIG. 1A

CCATGCCGGCCCCTCACAGCCCCGCCGGGAGCCCGAGCCCGCTGCCCAGGCTGGC
CGCCGCSGTGCCGATGTAGCGGGCTCCGGATCCCAGCCTCTCCCCTGCTCCCGTGC
TCTGCGGATCTCCCCTGACCGCTCTCCACAGCCCGGACCCGGGGGCTGGCCCAGG
GCCCTGCAGGCCCTGGCGTCCTGATGCCCCCAAGCTCCCTCTCCTGAGAAGCCACC
AGCACCACCCAGACTTGGGGGCAGGCGCCAGGGACGGACGTGGGCCAGTGCGAGC
CCAGAGGGCCCGAAGGCCGGGGCCCACCATGGCCCAAGCCCTGCCCTGGCTCCTG
CTGTGGATGGGCGCGGGAGTGCTGCCTGCCCACGGCACCCAGCACGGCATCCGGC
TGCCCCTGCGCAGCGGCCTGGGGGGCGCCCCCCTGGGGCTGCGGCTGCCCCGGG
AGACCGACGAAGAGCCCGAGGAGCCCGGCCGGAGGGGCAGCTTTGTGGAGATGGT
GGACAACCTGAGGGGCAAGTCGGGGCAGGGCTACTACGTGGAGATGACCGTGGGC
AGCCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTTTGCAGT
GGGTGCTGCCCCCCACCCCTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCA
CATACCGGGACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAA
GGGGAGCTGGGCACCGACCTGGTAAGCATCCCCCATGGCCCCAACGTCACTGTGCG
TGCCAACATTGCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCCAACTGG
GAAGGCATCCTGGGGCTGGCCTATGCTGAGATTGCCAGGCCTGACGACTCCCTGGA
GCCTTTCTTTGACTCTCTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAG
CTTTGTGGTGCTGGCTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTCGGAGG
GAGCATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATAC
ACCCATCCGGCGGGAGTGGTATTATGAGGTGATCATTGTGCGGGTGGAGATCAATG
GACAGGATCTGAAAATGGACTGCAAGGAGTACAACTATGACAAGAGCATTGTGGACA
GTGGCACCACCAACCTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGCAGTCAAATCCA
TCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGAGAGCAG
CTGGTGTGCTGGCAAGCAGGCACCACCCCTTGGAACATTTTCCCAGTCATCTCACTC
TACCTAATGGGTGAGGTTACCAACCAGTCCTTCCGCATCACCATCCTTCCGCAGCAA
TACCTGCGGCCAGTGGAAGATGTGGCCACGTCCCAAGACGACTGTTACAAGTTTGCC
ATCTCACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTAC
GTTGTCTTTGATCGGGCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGCCATGTG
CACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCTTTTGTCACCTTGGACATGGA
AGACTGTGGCTACAACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTA
TGTCATGGCTGCCATCTGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTCA
GTGGCGCTGCCTCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTGATGACATCT
CCCTGCTGAAGTGAGGAGGCCCATGGGCAGAAGATAGAGATTCCCCTGGACCACAC
CTCCGTGGTTCACTTTGGTCACAAGTAGGAGACACAGATGGCACCTGTGGCCAGAG
CACCTCAGGACCCTCCCCACCCACCAAATGCCTCTGCCTTGATGGAGAAGGAAAAG
GCTGGCAAGGTGGGTTCCAGGGACTGTACCTGTAGGAAACAGAAAAGAGAAGAAAG
AAGCACTCTGCTGGCGGGAATACTCTTGGTCACCTCAAATTTAAGTCGGGAAATTCT
GCTGCTTGAAACTTCAGCCCTGAACCTTTGTCCACCATTCCTTTAAATTCTCCAACCC
AAAGTATTCTTCTTTTCTTAGTTTCAGAAGTACTGGCATCACACGCAGGTTACCTTGG
CGTGTGTCCCTGTGGTACCCTGGCAGAGAAGAGACCAAGCTTGTTTCCCTGCTGGC
CAAAGTCAGTAGGAGAGGATGCACAGTTTGCTATTTGCTTTAGAGACAGGGACTGTA
TAAACAAGCCTAACATTGGTGCAAAGATTGCCTCTTGAATT

FIG. 1B

MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLGLRLP
RETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQT
LNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVPY
TQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFINGSNWE
GILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQLCGAGFPLN
QSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRVEIN
GQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIKAASST
EKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRIT
ILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVV
FDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQ
TDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQQHDDF
ADDISLLK

FIG. 2A

METDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQT
LNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVPY
TQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFINGSNWE
GILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQLCGAGFPLN
QSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRVEIN
GQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIKAASST
EKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRIT
ILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVV
FDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQ
TDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQQHDDF
ADDISLLK

FIG. 2B

FIG. 3A

MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLGLRLPRETDEEPE
EPGRRGSFVEMVDNLRGKSGQGYYVEMT
VGSPPQTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVPYT
QGKWEGELGTDLVSIPHGPNVTVRANI
AAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQL
CGAGFPLNQSEVLASVGGSMIIGGI
DHSLYTGSLWYTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNL
RLPKKVFEAAVKSIKAASSTEKFPD
GFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVA
TSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQTDED
YKDDDDK

FIG. 3B

ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMT
VGSPPQTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVPYT
QGKWEGELGTDLVSIPHGPNVTVRANI
AAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQL
CGAGFPLNQSEVLASVGGSMIIGGI
DHSLYTGSLWYTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNL
RLPKKVFEAAVKSIKAASSTEKFPD
GFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVA
TSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQTDED
YKDDDDK
C

FIG. 4

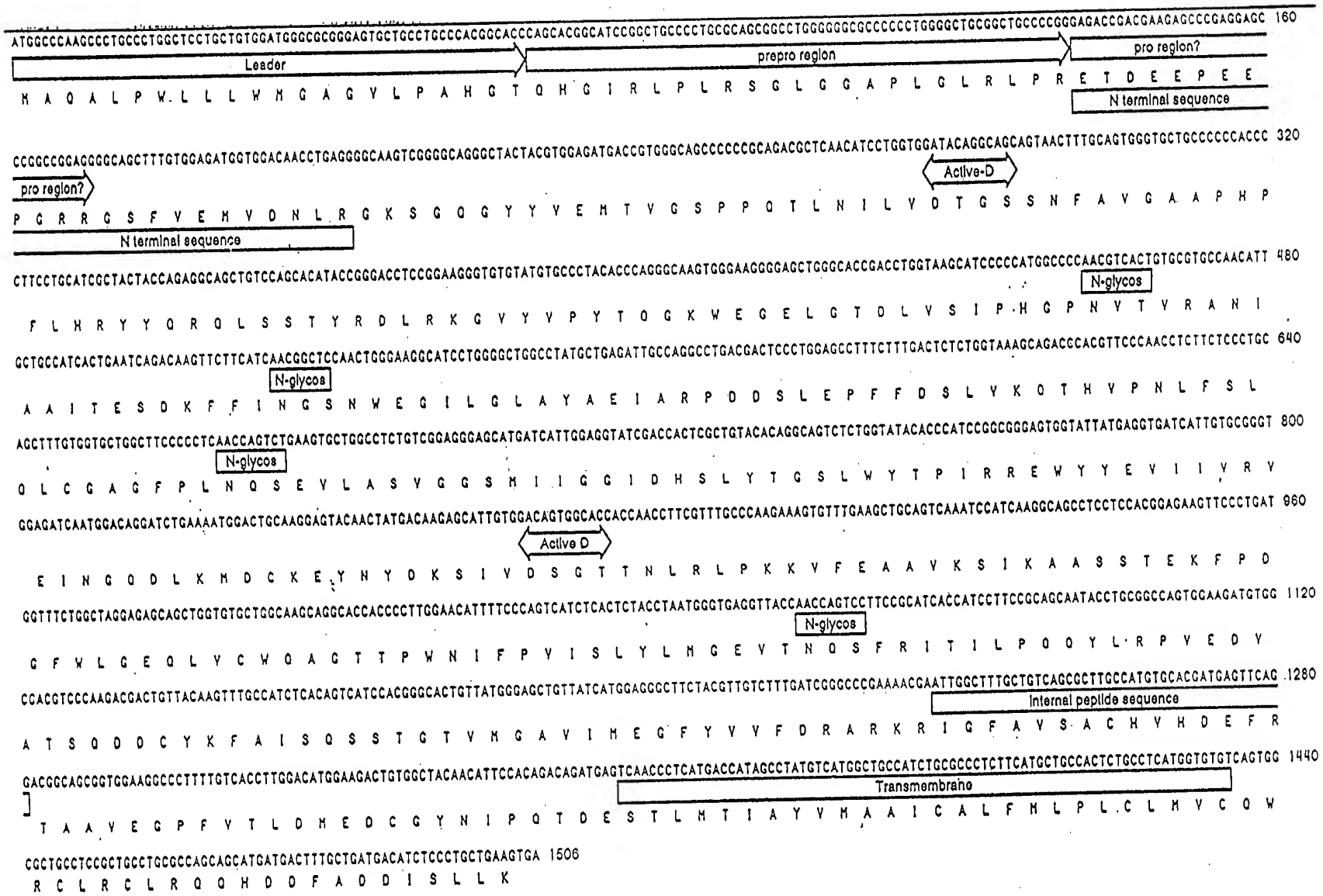
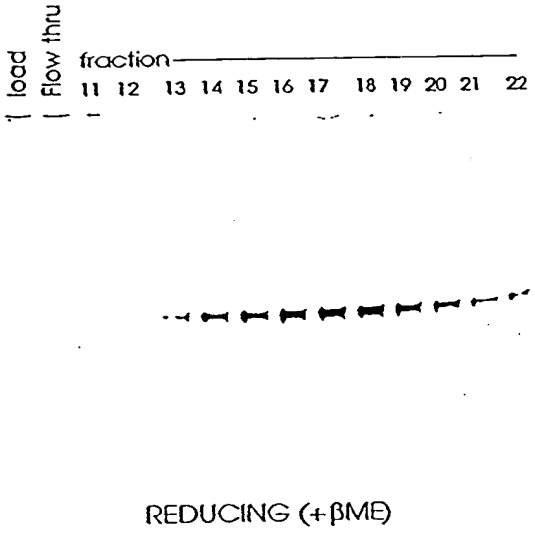
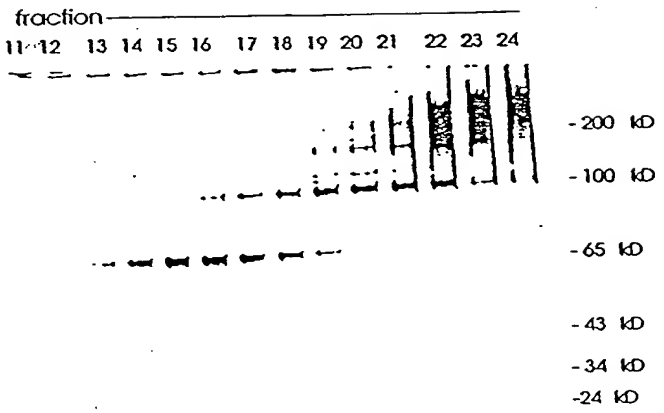

Leader
prepro region
pro region?
N terminal sequence
Active-D
pro region?
N terminal sequence
N-glycos
N-glycos
N-glycos
Active D
N-glycos
Internal peptide sequence
Transmembrane

FIG. 5



REDUCING (+βME)

FIG. 6A



NONREDUCING (NCβME)

FIG. 6B

FIG. 7

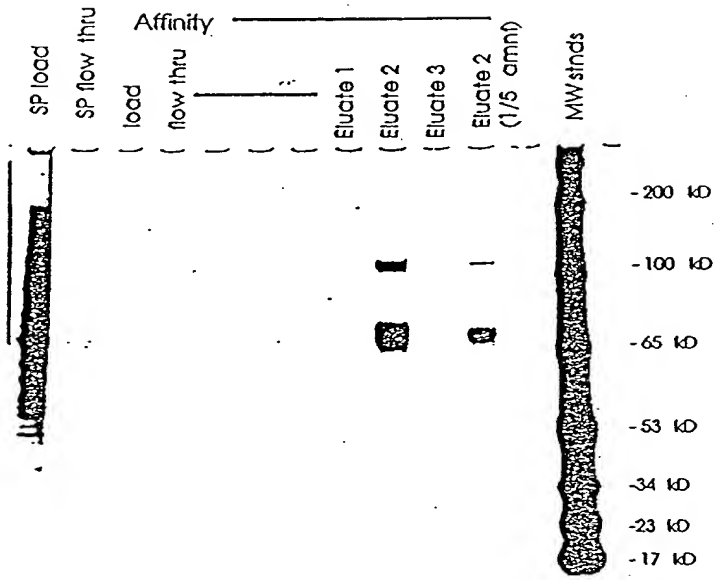
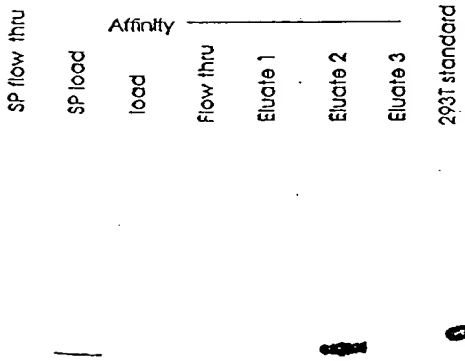

SP load
SP flow thru
Affinity
load
flow thru
Eluate 1
Eluate 2
Eluate 3
Eluate 2 (1/5 amnt)
MW stnds
-200 kD
-100 kD
-65 kD
-53 kD
-34 kD
-23 kD
-17 kD

FIG. 8


SP flow thru
SP load
Affinity
load
flow thru
Eluate 1
Eluate 2
Eluate 3
293T standard

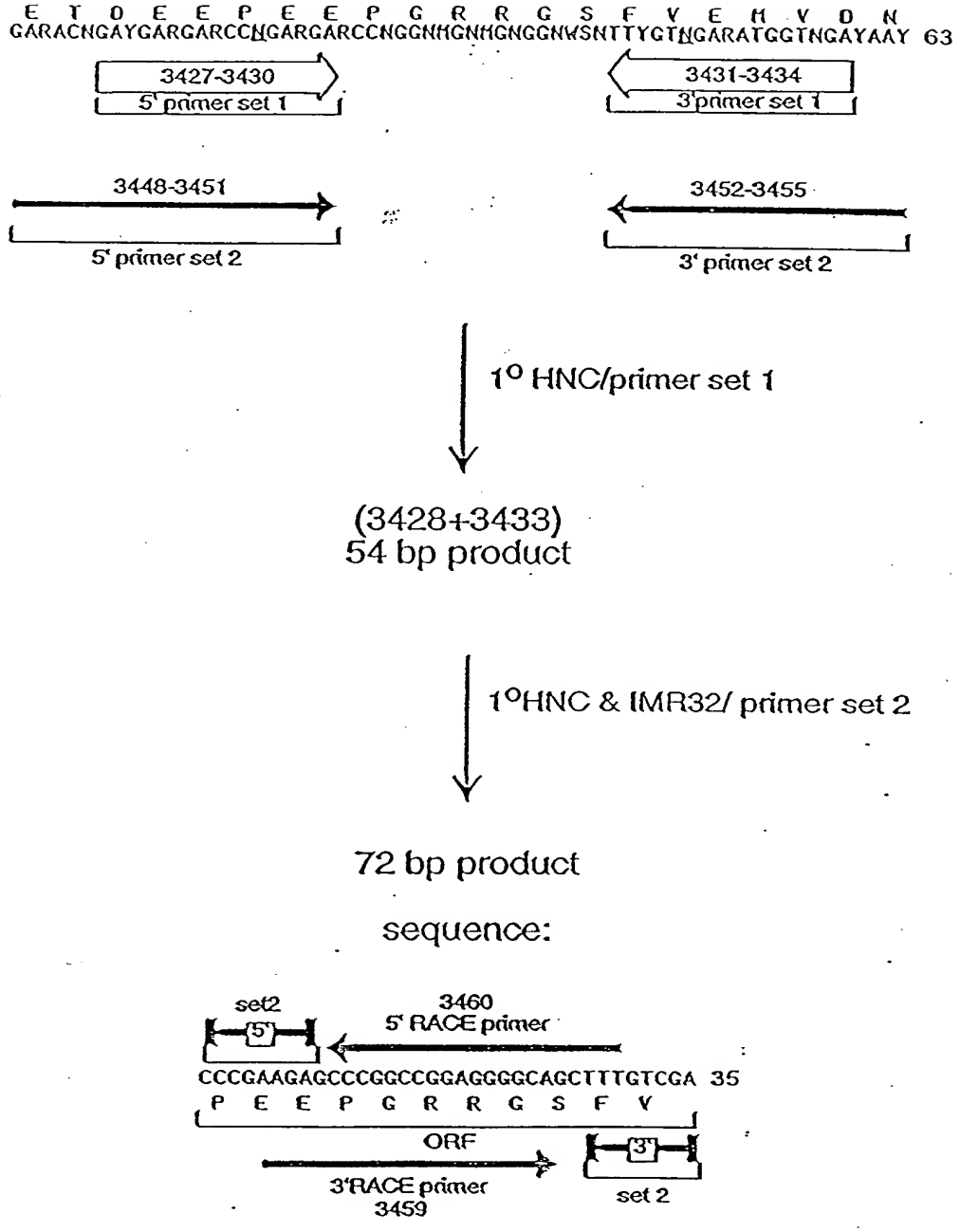
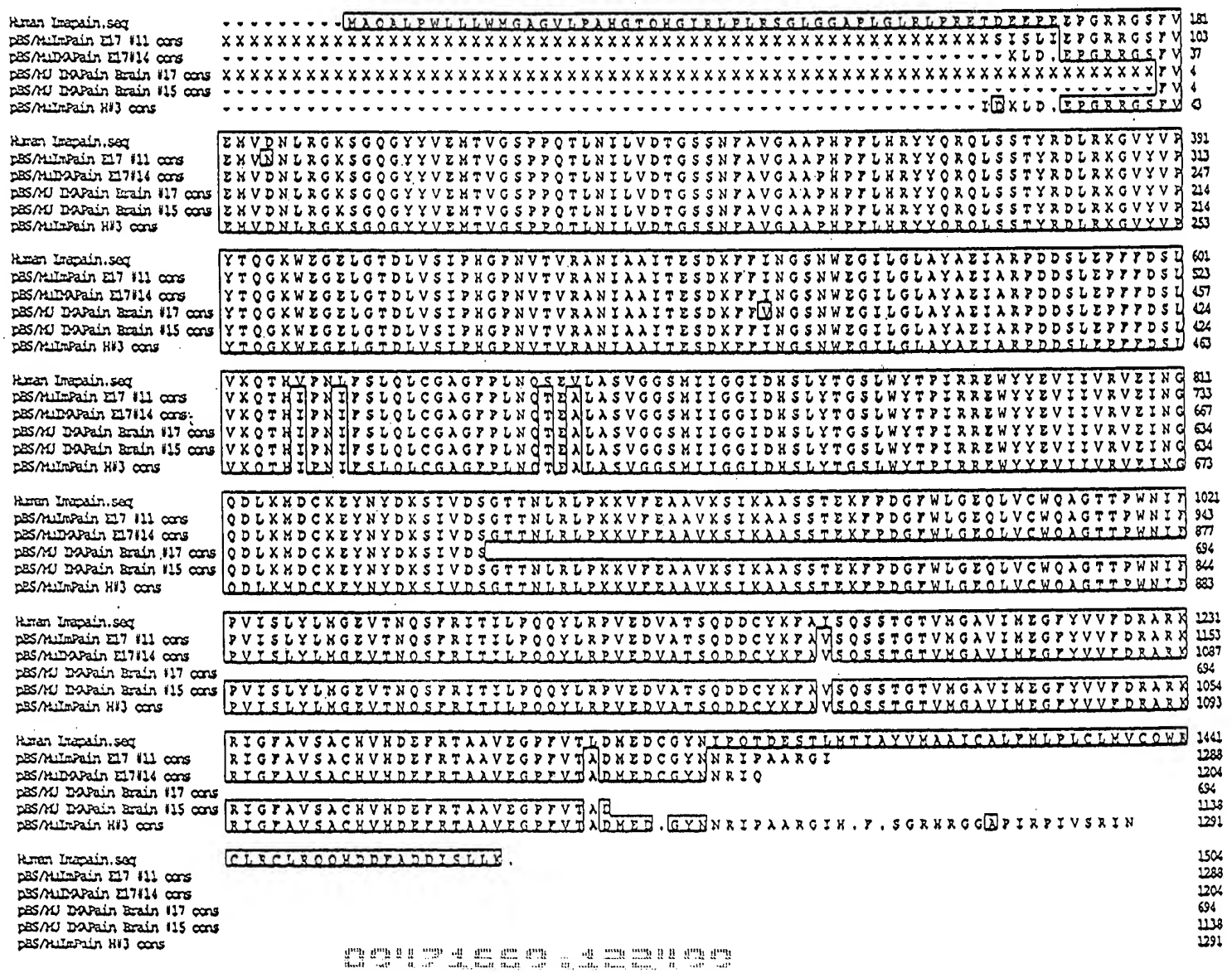

E T D E E P E E P G R R G S F V E M V D N
GARACNGAYGARGARCCNGARGARCCNGGNMGNMGNGGNWSNTTYGTNGARATGGTNGAYAAY 63
3427-3430
5' primer set 1
3431-3434
3'primer set 1
3448-3451
5' primer set 2
3452-3455
3' primer set 2
1° HNC/primer set 1
(3428+3433)
54 bp product
1°HNC & IMR32/ primer set 2
72 bp product
sequence:
set2
5'
3460
5' RACE primer
CCCGAAGAGCCCGGCCGGAGGGGCAGCTTTGTCGA 35
P E E P G R R G S F V
ORF
3'
3'RACE primer
3459
set 2

FIG. 9

FIG. 10



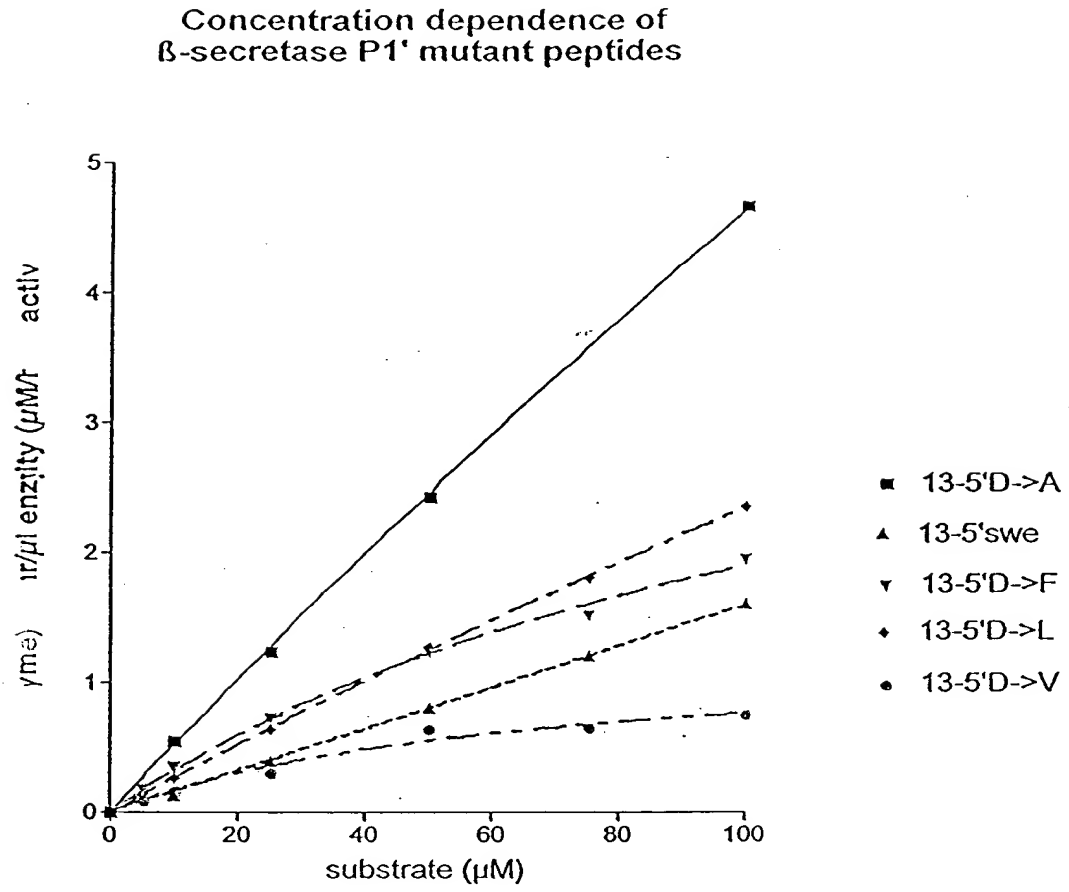

Concentration dependence of
ß-secretase P1' mutant peptides
activ
(μM/r
enzyity
ır/μl
γmə)
substrate (μM)
0
20
40
60
80
100
1
2
3
4
5
13-5'D->A
13-5'swe
13-5'D->F
13-5'D->L
13-5'D->V

FIG. 11

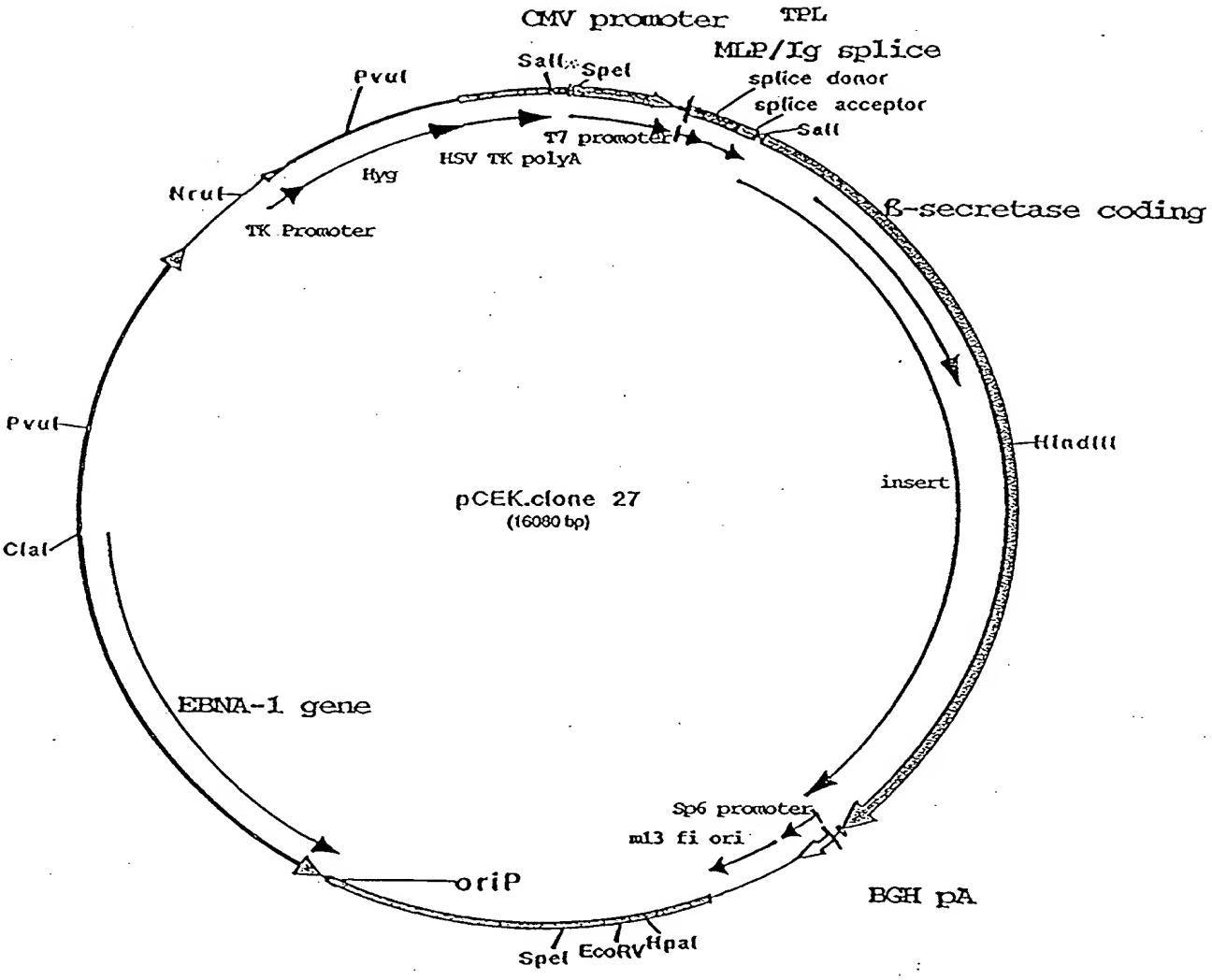

CMV promoter
TPL
MLP/Ig splice
splice donor
splice acceptor
SalI
SpeI
PvuI
T7 promoter
HSV TK polyA
Hyg
NruI
TK Promoter
ß-secretase coding
PvuI
HindIII
insert
pCEK.clone 27
(16080 bp)
ClaI
EBNA-1 gene
Sp6 promoter
m13 fi ori
oriP
BGH pA
SpeI
EcoRV
HpaI

FIG. 12

FIG. 13A

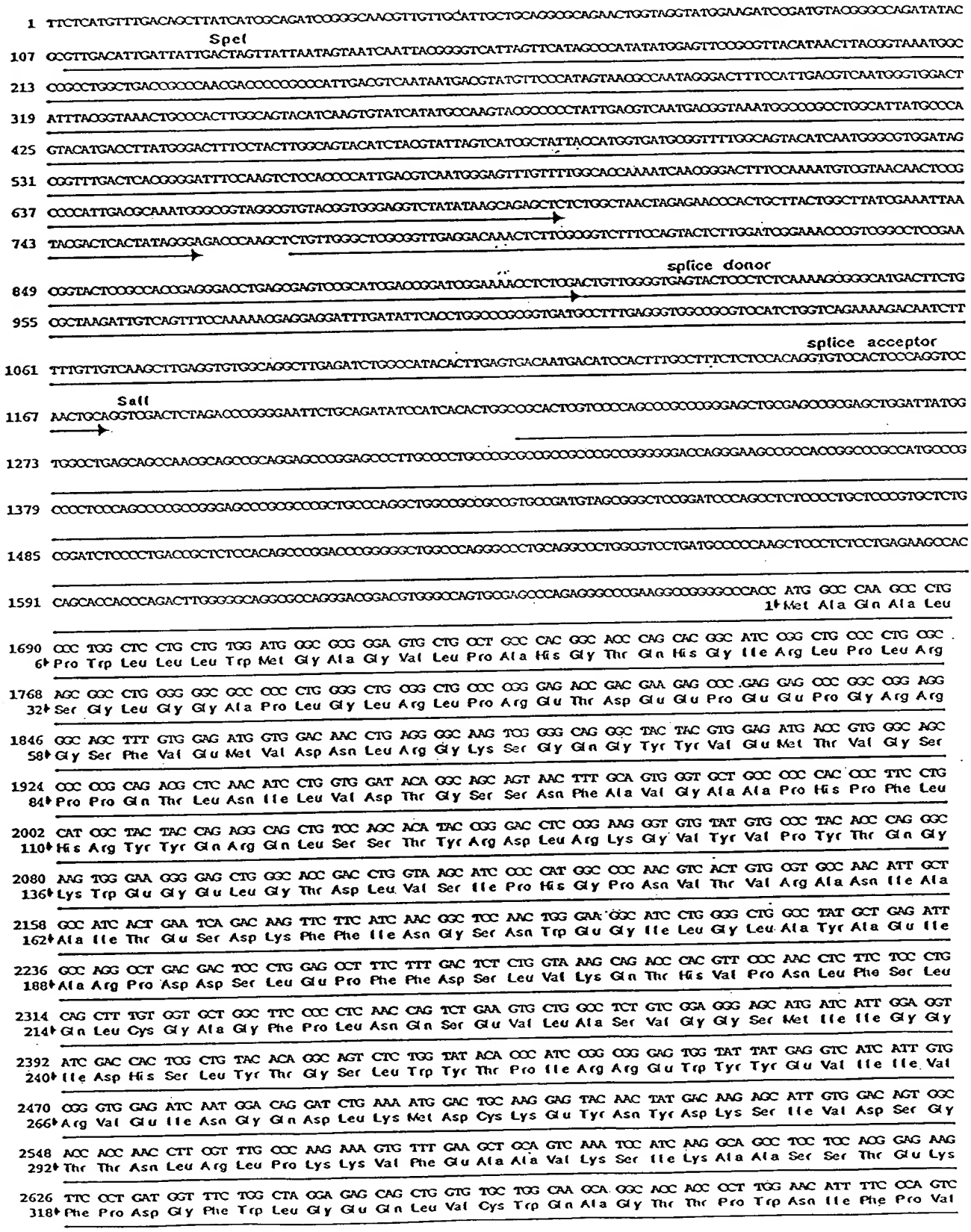


FIG. 13B

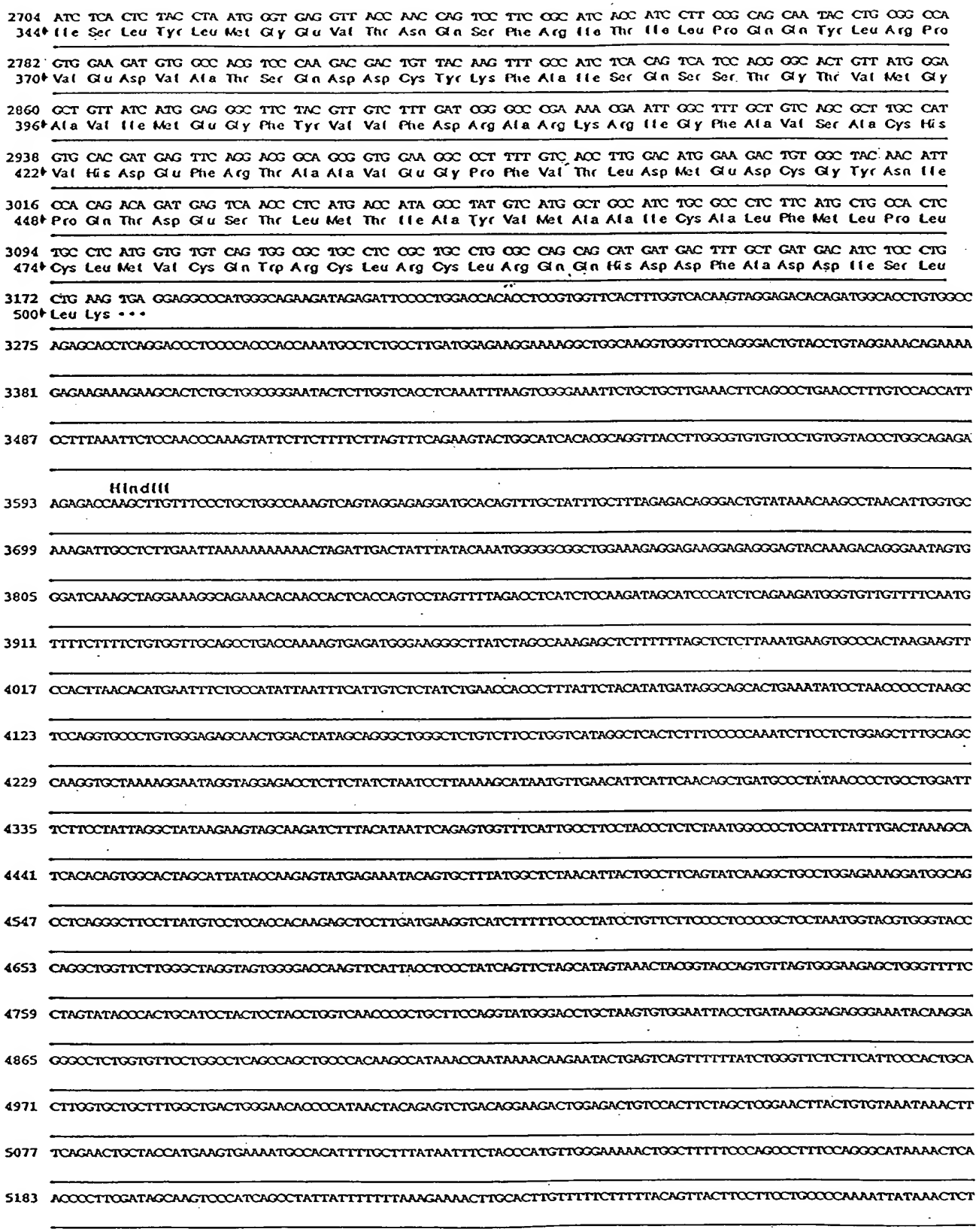
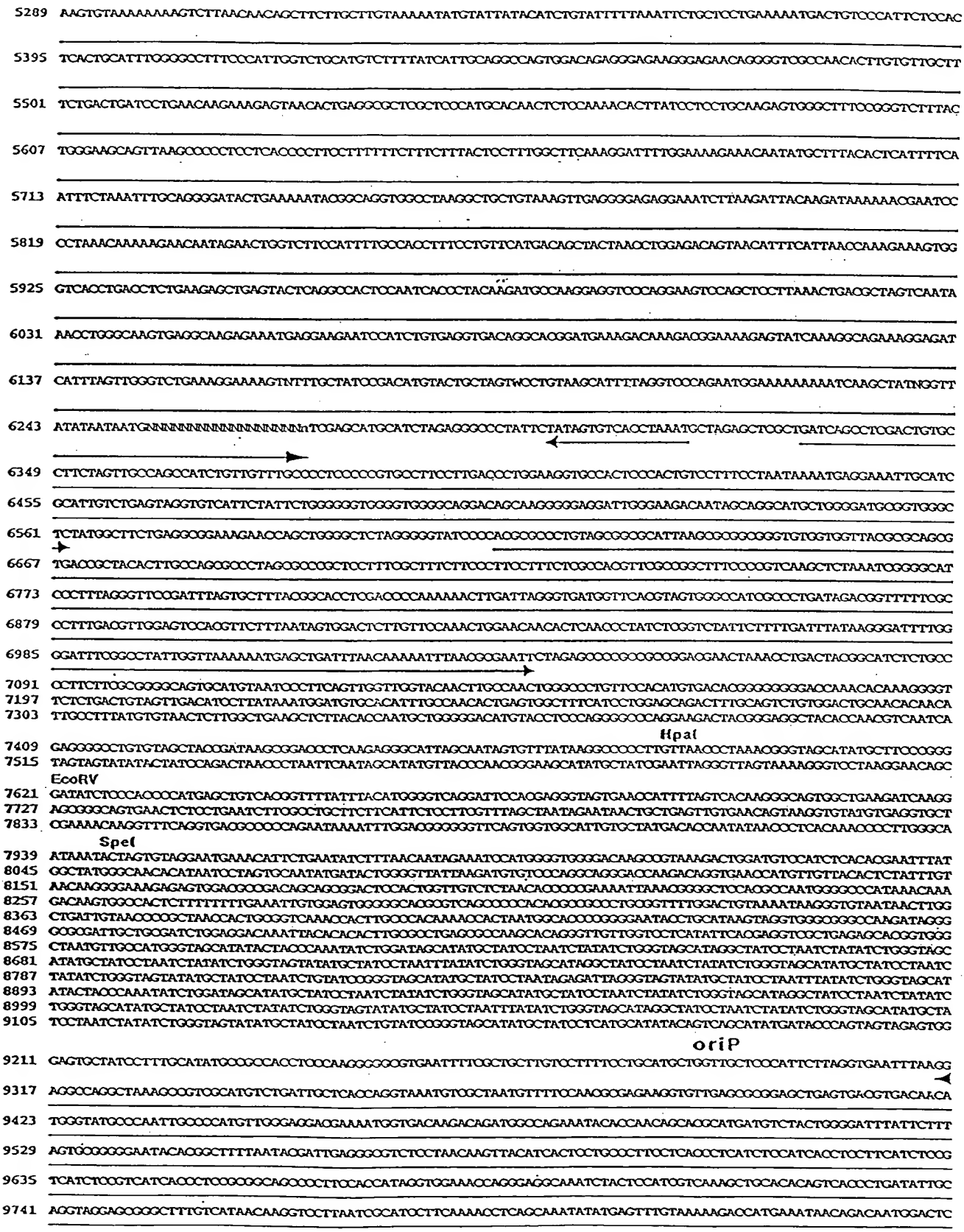

2704 ATC TCA CTC TAC CTA ATG GGT GAG GTT ACC AAC CAG TCC TTC CGC ATC AGC ATC CTT CGG CAG CAA TAC CTG CGG CCA
344 Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro
2782 GTG GAA GAT GTG GCC AGG TCC CAA GAC GAC TGT TAC AAG TTT GCC ATC TCA CAG TCA TCC AGG GGC ACT GTT ATG GGA
370 Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly
2860 GCT GTT ATC ATG GAG GGC TTC TAC GTT GTC TTT GAT CGG GCC CGA AAA CGA ATT GGC TTT GCT GTC AGC GCT TGC CAT
396 Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His
2938 GTG CAC GAT GAG TTC AGG AGG GCA GGG GTG GAA GGC CCT TTT GTC ACC TTG GAC ATG GAA GAC TGT GGC TAC AAC ATT
422 Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile
3016 CCA CAG ACA GAT GAG TCA ACC CTC ATG ACC ATA GGC TAT GTC ATG GCT GGC ATC TGC GGC CTC TTC ATG CTG CCA CTC
448 Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu
3094 TGC CTC ATG GTG TGT CAG TGG CGC TGC CTC CGC TGC CTG CGC CAG CAG CAT GAT GAC TTT GCT GAT GAC ATC TCC CTG
474 Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser Leu
3172 CTG AAG TGA GGAGGCCCATGGGCAGAAGATAGAGATTCCCCTGGACCACACCTCCGTGGTTCACTTTGGTCACAAGTAGGAGACACAGATGGCACCTGTGGCC
500 Leu Lys ***
3275 AGAGCACCTCAGGACCCTCCCCACCCACCAAATGCCTCTGCCTTGATGGAGAAGGAAAAGGCTGGCAAGGTGGGTTCCAGGGACTGTACCTGTAGGAAACAGAAAA
3381 GAGAAGAAAGAAGCACTCTGCTGGCGGGAATACTCTTGGTCACCTCAAATTTAAGTCGGGAAATTCTGCTGCTTGAAACTTCAGCCCTGAACCTTTGTCCACCATT
3487 CCTTTAAATTCTCCAACCCAAAGTATTCTTCTTTTCTTAGTTTCAGAAGTACTGGCATCACACGCAGGTTACCTTGGCGTGTGTCCCTGTGGTACCCTGGCAGAGA
HindIII
3593 AGAGACCAAGCTTGTTTCCCTGCTGGCCAAAGTCAGTAGGAGAGGATGCACAGTTTGCTATTTGCTTTAGAGACAGGGACTGTATAAACAAGCCTAACATTGGTGC
3699 AAAGATTGCCTCTTGAATTAAAAAAAAAAAACTAGATTGACTATTTATACAAATGGGGGCGGCTGGAAAGAGGAGAAGGAGAGGGAGTACAAAGACAGGGAATAGTG
3805 GGATCAAAGCTAGGAAAGGCAGAAACACAACCACTCACCAGTCCTAGTTTTAGACCTCATCTCCAAGATAGCATCCCATCTCAGAAGATGGGTGTTGTTTTCAATG
3911 TTTTCTTTTCTGTGGTTGCAGCCTGACCAAAAGTGAGATGGGAAGGGCTTATCTAGCCAAAGAGCTCTTTTTTAGCTCTCTTAAATGAAGTGCCCACTAAGAAGTT
4017 CCACTTAACACATGAATTTCTGCCATATTAATTTCATTGTCTCTATCTGAACCACCCTTTATTCTACATATGATAGGCAGCACTGAAATATCCTAACCCCCTAAGC
4123 TCCAGGTGCCCTGTGGGAGAGCAACTGGACTATAGCAGGGCTGGGCTCTGTCTTCCTGGTCATAGGCTCACTCTTTCCCCCAAATCTTCCTCTGGAGCTTTGCAGC
4229 CAAGGTGCTAAAAGGAATAGGTAGGAGACCTCTTCTATCTAATCCTTAAAAGCATAATGTTGAACATTCATTCAACAGCTGATGCCCTATAACCCCTGCCTGGATT
4335 TCTTCCTATTAGGCTATAAGAAGTAGCAAGATCTTTACATAATTCAGAGTGGTTTCATTGCCTTCCTACCCTCTCTAATGGCCCCTCCATTTATTTGACTAAAGCA
4441 TCACACAGTGGCACTAGCATTATACCAAGAGTATGAGAAATACAGTGCTTTATGGCTCTAACATTACTGCCTTCAGTATCAAGGCTGCCTGGAGAAAGGATGGCAG
4547 CCTCAGGGCTTCCTTATGTCCTCCACCACAAGAGCTCCTTGATGAAGGTCATCTTTTTCCCCTATCCTGTTCTTCCCCTCCCCGCTCCTAATGGTAGGTGGGTACC
4653 CAGGCTGGTTCTTGGGCTAGGTAGTGGGGACCAAGTTCATTACCTCCCTATCAGTTCTAGCATAGTAAACTACGGTACCAGTGTTAGTGGGAAGAGCTGGGTTTTC
4759 CTAGTATACCCACTGCATCCTACTCCTACCTGGTCAACCCGCTGCTTCCAGGTATGGGACCTGCTAAGTGTGGAATTACCTGATAAGGGAGAGGGAAATACAAGGA
4865 GGGCCTCTGGTGTTCCTGGCCTCAGCCAGCTGCCCACAAGCCATAAACCAATAAAACAAGAATACTGAGTCAGTTTTTTATCTGGGTTCTCTTCATTCCCACTGCA
4971 CTTGGTGCTGCTTTGGCTGACTGGGAACACCCCATAACTACAGAGTCTGACAGGAAGACTGGAGACTGTCCACTTCTAGCTCGGAACTTACTGTGTAAATAAACTT
5077 TCAGAACTGCTACCATGAAGTGAAAATGCCACATTTTGCTTTATAATTTCTACCCATGTTGGGAAAAACTGGCTTTTTCCCAGCCCTTTCCAGGGCATAAAACTCA
5183 ACCCCTTCGATAGCAAGTCCCATCAGCCTATTATTTTTTTAAAGAAAACTTGCACTTGTTTTTCTTTTTACAGTTACTTCCTTCCTGCCCCAAAATTATAAACTCT

FIG. 13C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5395 TCACTGCATTTGGGGCCTTTCCCATTGGTCTGCATGTCTTTTATCATTGCAGGCCAGTGGACAGAGGGAGAAGGGAGAACAGGGGTCGCCAACACTTGTGTTGCTT
5501 TCTGACTGATCCTGAACAAGAAAGAGTAACACTGAGGCGCTCGCTCCCATGCACAACTCTCCAAAACACTTATCCTCCTGCAAGAGTGGGCTTTCCGGGTCTTTAC
5607 TGGGAAGCAGTTAAGCCCCCTCCTCACCCCTTCCTTTTTTCTTTCTTTACTCCTTTGGCTTCAAAGGATTTTGGAAAAGAAACAATATGCTTTACACTCATTTTCA
5713 ATTTCTAAATTTGCAGGGGATACTGAAAAATACGGCAGGTGGCCTAAGGCTGCTGTAAAGTTGAGGGGAGAGGAAATCTTAAGATTACAAGATAAAAAAACGAATCC
5819 CCTAAACAAAAAGAACAATAGAACTGGTCTTCCATTTTGCCACCTTTCCTGTTCATGACAGCTACTAACCTGGAGACAGTAACATTTCATTAACCAAAGAAAGTGG
5925 GTCACCTGACCTCTGAAGAGCTGAGTACTCAGGCCACTCCAATCACCCTACAAGATGCCAAGGAGGTCCCAGGAAGTCCAGCTCCTTAAACTGACGCTAGTCAATA
6031 AACCTGGGCAAGTGAGGCAAGAGAAATGAGGAAGAATCCATCTGTGAGGTGACAGGCACGGATGAAAGACAAAGACGGAAAAGAGTATCAAAGGCAGAAAGGAGAT
6137 CATTTAGTTGGGTCTGAAAGGAAAAGTNTTTGCTATCCGACATGTACTGCTAGTWCCTGTAAGCATTTTAGGTCCCAGAATGGAAAAAAAAAATCAAGCTATNGGTT
6243 ATATAATAATGNNNNNNNNNNNNNNNNNnTCGAGCATGCATCTAGAGGGCCCTATTCTATAGTGTCACCTAAATGCTAGAGCTCGCTGATCAGCCTCGACTGTGC
6349 CTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAATTGCATC
6455 GCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGC
6561 TCTATGGCTTCTGAGGCGGAAAGAACCAGCTGGGGCTCTAGGGGGTATCCCCACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCG
6667 TGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGCAT
6773 CCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGC
6879 CCTTTGACGTTGGAGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGG
6985 GGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTCTAGAGCCCCCGCCGCGGACGAACTAAACCTGACTACGGCATCTCTGCC
7091 CCTTCTTGCGGGGCAGTGCATGTAATCCCTTCAGTTGGTTGGTACAACTTGCCAACTGGGCCCTGTTCCACATGTGACACGGGGGGGGGACCAAACACAAAGGGGT
7197 TCTCTGACTGTAGTTGACATCCTTATAAATGGATGTGCACATTTGCCAACACTGAGTGGCTTTCATCCTGGAGCAGACTTTGCAGTCTGTGGACTGCAACACAACA
7303 TTGCCTTTATGTGTAACTCTTGGCTGAAGCTCTTACACCAATGCTGGGGGACATGTACCTCCCAGGGCCCCAGGAAGACTACGGGAGGCTACACCAACGTCAATCA
Hpal
7409 GAGGGGCCTGTGTAGCTACCGATAAGCGGACCCTCAAGAGGGCATTAGCAATAGTGTTTATAAGGCCCCCTTGTTAACCCTAAACGGGTAGCATATGCTTCCCCGGG
7515 TAGTAGTATATACTATCCAGACTAACCCTAATTCAATAGCATATGTTACCCAACGGGAAGCATATGCTATCGAATTAGGGTTAGTAAAAGGGTCCTAAGGAACAGC
EcoRV
7621 GATATCTCCCACCCCATGAGCTGTCACGGTTTTATTTACATGGGGTCAGGATTCCACGAGGGTAGTGAACCATTTTAGTCACAAGGGCAGTGGCTGAAGATCAAGG
7727 AGCGGGCAGTGAACTCTCCTGAATCTTGGCCTGCTTCTTCATTCTCCTTGGTTTAGCTAATAGAATAACTGCTGAGTTGTGAACAGTAAGGTGTATGTGAGGTGCT
7833 CGAAAACAAGGTTTCAGGTGACGCCCCCAGAATAAAATTTGGACGGGGGGTTCAGTGGTGGCATTGTGCTATGACACCAATATAACCCTCACAAACCCCTTGGGCA
SpeI
7939 ATAAATACTAGTGTAGGAATGAAACATTCTGAATATCTTTAACAATAGAAATCCATGGGGTGGGGACAAGCGGTAAAGACTGGATGTCCATCTCACACGAATTTAT
8045 GGCTATGGGCAACACATAATCCTAGTGCAATATGATACTGGGGTTATTAAGATGTGTCCCAGGCAGGGACCAAGACAGGTGAACCATGTTGTTACACTCTATTTGT
8151 AACAAGGGGAAAGAGAGTGGAGCGCGACAGCAGCGGACTCCACTGGTTGTCTCTAACACCCCGAAAATTAAACGGGGCTCCACGCCAATGGGGCCCATAAACAAA
8257 GACAAGTGGCCACTCTTTTTTTTGAAATTGTGGAGTGGGGGCAGCGGTCAGCCCCCACACGCCGCCCTGCGGTTTTGGACTGTAAAATAAGGGTGTAATAACTTGG
8363 CTGATTGTAACCCCGCTAACCACTGCGGTCAAACCACTTGCCCACAAAACCACTAATGGCACCCCGGGGAATACCTGCATAAGTAGGTGGGCGGGCCAAGATAGGG
8469 GCGCGATTGCTGCGATCTGGAGGACAAATTACACACACTTGCGCCTGAGCGCCAAGCACAGGGTTGTTGGTCCTCATATTCACGAGGTCGCTGAGAGCACGGTGGG
8575 CTAATGTTGCCATGGGTAGCATATACTACCCAAATATCTGGATAGCATATGCTATCCTAATCTATATCTGGGTAGCATAGGCTATCCTAATCTATATCTGGGTAGC
8681 ATATGCTATCCTAATCTATATCTGGGTAGTATATGCTATCCTAATTTATATCTGGGTAGCATAGGCTATCCTAATCTATATCTGGGTAGCATATGCTATCCTAATC
8787 TATATCTGGGTAGTATATGCTATCCTAATCTGTATCCGGGTAGCATATGCTATCCTAATAGAGATTAGGGTAGTATATGCTATCCTAATTTATATCTGGGTAGCAT
8893 ATACTACCCAAATATCTGGATAGCATATGCTATCCTAATCTATATCTGGGTAGCATATGCTATCCTAATCTATATCTGGGTAGCATAGGCTATCCTAATCTATATC
8999 TGGGTAGCATATGCTATCCTAATCTATATCTGGGTAGTATATGCTATCCTAATTTATATCTGGGTAGCATAGGCTATCCTAATCTATATCTGGGTAGCATATGCTA
9105 TCCTAATCTATATCTGGGTAGTATATGCTATCCTAATCTGTATCCGGGTAGCATATGCTATCCTCATGCATATACAGTCAGCATATGATACCCAGTAGTAGAGTGG
oriP
9211 GAGTGCTATCCTTTGCATATGCCGCCACCTCCCAAGGGGCGGTGAATTTTCGCTGCTTGTCCTTTTCCTGCATGCTGGTTGCTCCCATTCTTAGGTGAATTTAAGG
9317 AGGCCAGGCTAAAGCCGTCGCATGTCTGATTGCTCACCAGGTAAATGTCGCTAATGTTTTCCAAGCGCAGAAGGTGTTGAGCGCGGAGCTGAGTGACGTGACAACA
9423 TGGGTATGCCCAATTGCCCCATGTTGGGAGGACGAAAATGGTGACAAGACAGATGGCCAGAAATACACCAACAGCACGCATGATGTCTACTGGGGATTTATTCTTT
9529 AGTGCGGGGGAATACACGGCTTTTAATACGATTGAGGGCGTCTCCTAACAAGTTACATCACTCCTGCGCCTTCCTCACCCTCATCTCCATCACCTCCTTCATCTCCG
9635 TCATCTCCGTCATCACCCTCCGCCGCAGCCCCTTCCACCATAGGTGGAAACCAGGGAGGCAAATCTACTCCATGGTCAAAGCTGCACACAGTCACCCTGATATTGC
9741 AGGTAGGAGCGGGCTTTGTCATAACAAGGTCCTTAATCGCATCTTCAAAACCTCAGCAAATATATGAGTTTGTAAAAAGACCATGAAATAACAGACAATGGACTC

FIG. 13D

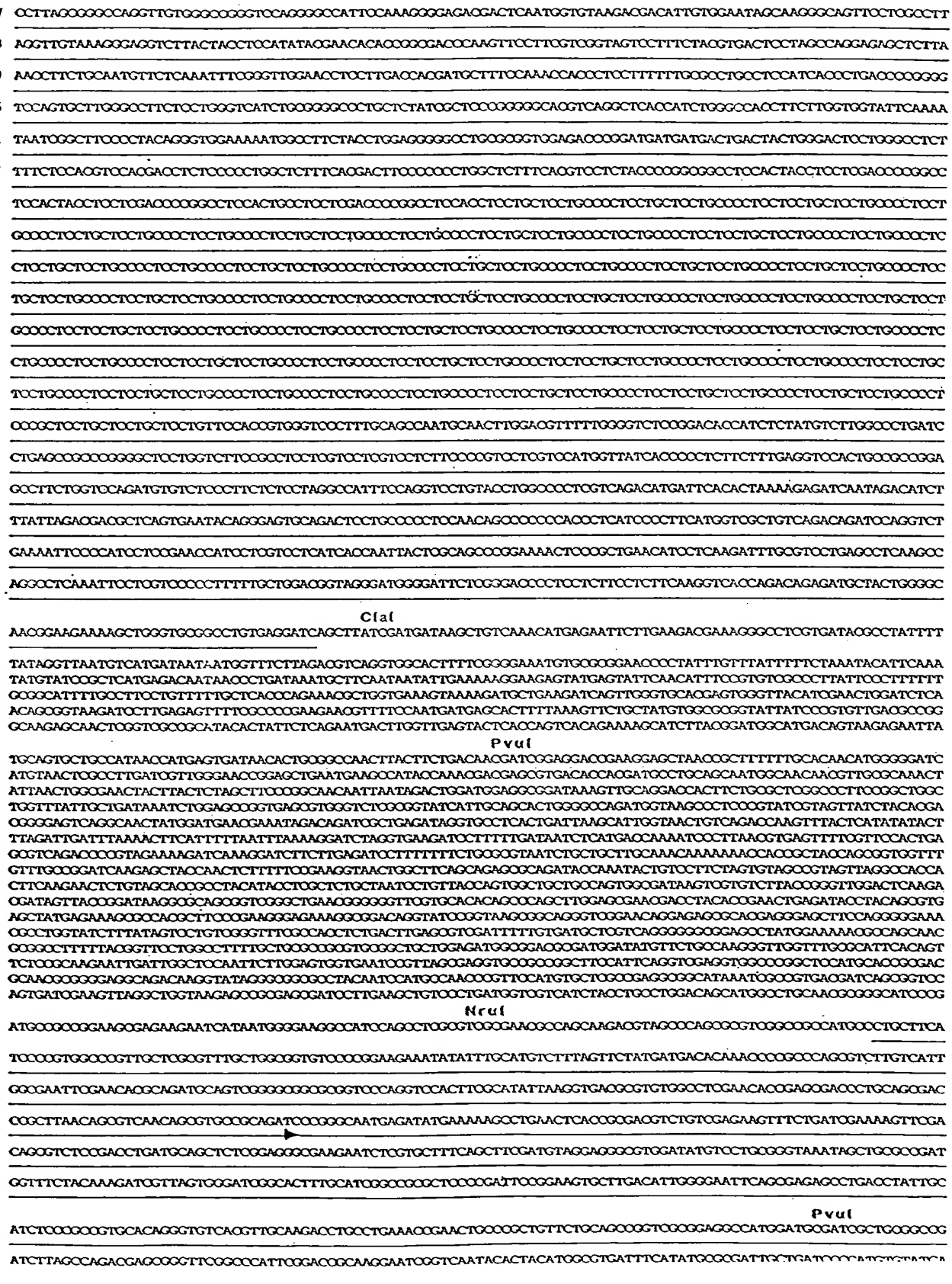
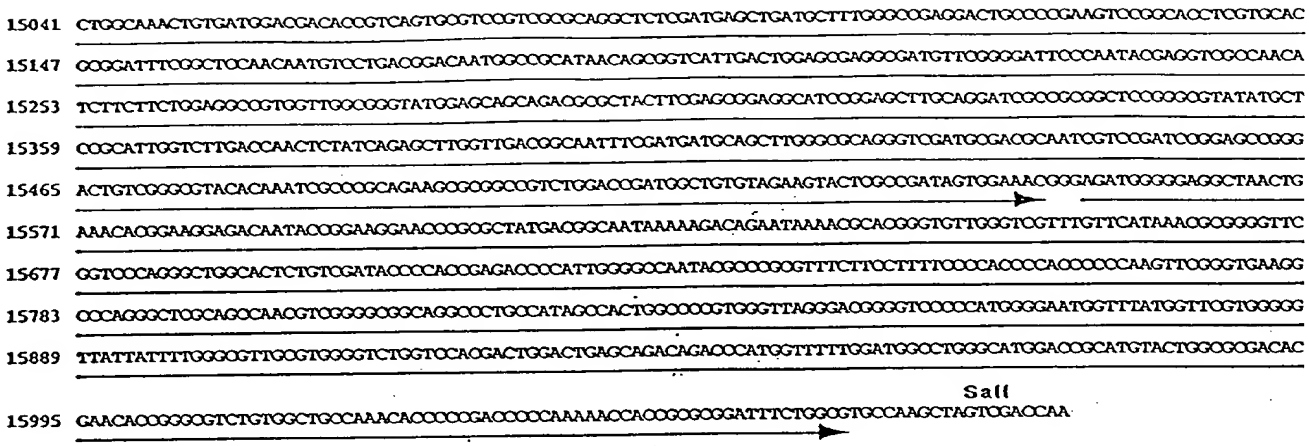


FIG. 13E


15041 CTGGCAAACTGTGATGGACGACACCGTCAGTGGGTCCGTCGGCGCAGGCTCTCGATGAGCTGATGCTTTGGGCCGAGGACTGCCCCGAAGTCCGGCACCTCGTGCAC
15147 GGGGATTTCGGCTCCAACAATGTCCTGACGGACAATGGCCGCATAACAGCGGTCATTGACTGGAGCGAGGCGATGTTCGGGGATTCCCAATACGAGGTCGCCAACA
15253 TCTTCTTCTGGAGGCCGTGGTTGGCGGGTATGGAGCAGCAGACGCGCTACTTCGAGCGGAGGCATCCGGAGCTTGCAGGATCGCCGCGGCTCCGGGCGTATATGCT
15359 CGGCATTGGTCTTGACCAACTCTATCAGAGCTTGGTTGACGGCAATTTCGATGATGCAGCTTGGGCGCAGGGTCGATGCGACGCAATCGTCCGATCCGGAGCCGGG
15465 ACTGTCGGGCGTACACAAATCGCCCGCAGAAGCGCGGCCGTCTGGACCGATGGCTGTGTAGAAGTACTCGCCGATAGTGGAAACCGACGCCGAGATGGGGGAGGCTAACTG
15571 AAACACGGAAGGAGACAATACCGGAAGGAACCCGCGCTATGACGGCAATAAAAAGACAGAATAAAACGCACGGGTGTTGGGTCGTTTGTTCATAAACGCGGGGGTTC
15677 GGTCCCAGGGCTGGCACTCTGTCGATACCCCACCGAGACCCCATTGGGGCCAATACGCCCGCGTTTCTTCCTTTTCCCCACCCCACGCCCCAAGTTCGGGTGAAGG
15783 CCCAGGGCTCGCAGCCAACGTCGGGGCGGCAGGCCCTGCCATAGCCACTGGCCCCGTGGGTTAGGGACGGGGTCCCCCATGGGGAATGGTTTATGGTTCGTGGGGG
15889 TTATTATTTTGGGCGTTGCGTGGGGTCTGGTCCACGACTGGACTGAGCAGACAGACCCATGGTTTTTGGATGGCCTGGGCATGGACCGCATGTACTGGCGCGACAC
Sall
15995 GAACACCGGGCGTCTGTGGCTGCCAAACACCCCCGACCCCCAAAAACCACCGCGCGGATTTCTGGCGTGCCAAGCTAGTCGACCAA

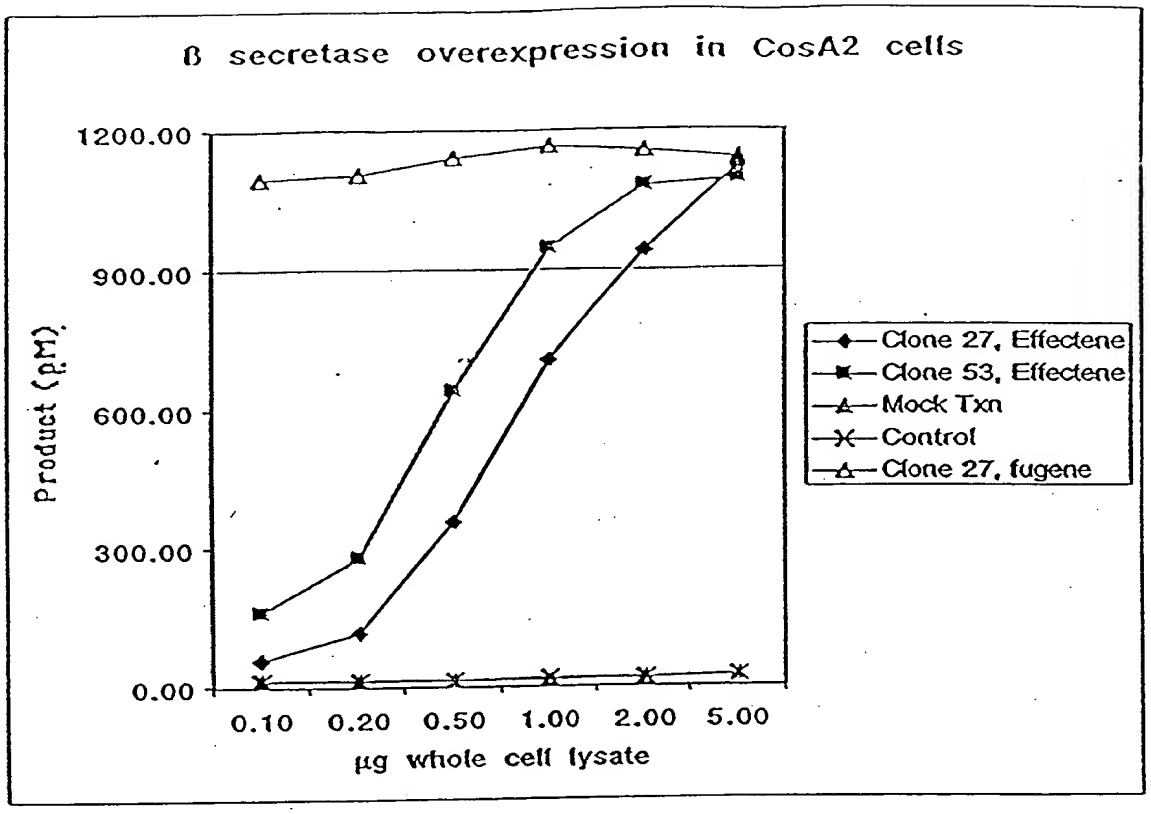

ß secretase overexpression in CosA2 cells
1200.00
900.00
600.00
300.00
0.00
Product (pM)
0.10
0.20
0.50
1.00
2.00
5.00
µg whole cell lysate
Clone 27, Effectene
Clone 53, Effectene
Mock Txn
Control
Clone 27, fugene

FIG. 14

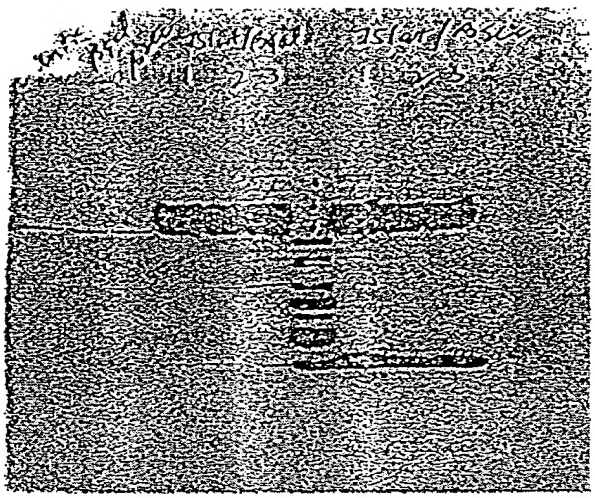


FIG. 15A

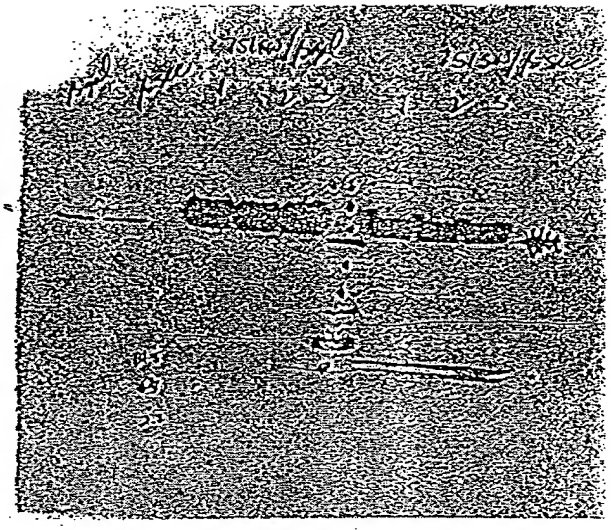


FIG. 15B

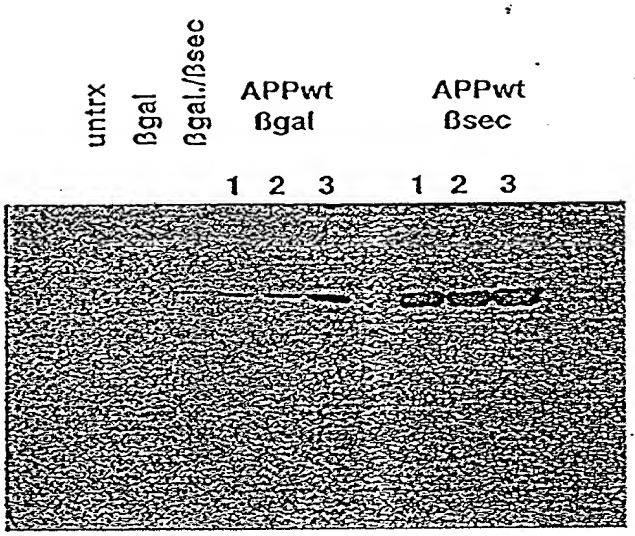


FIG. 16A

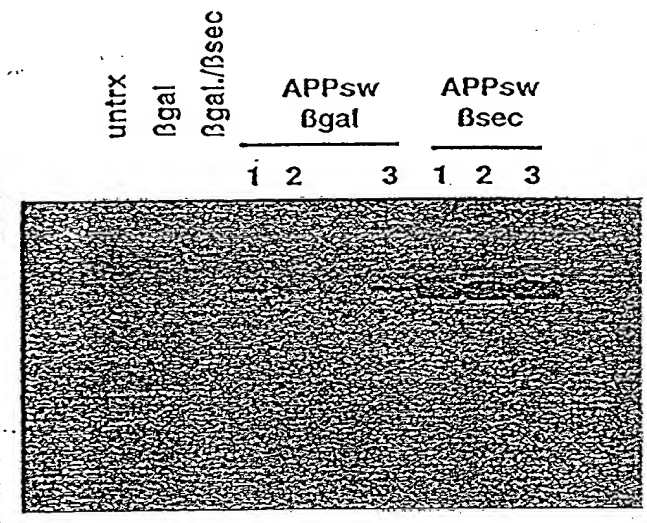


FIG. 16B

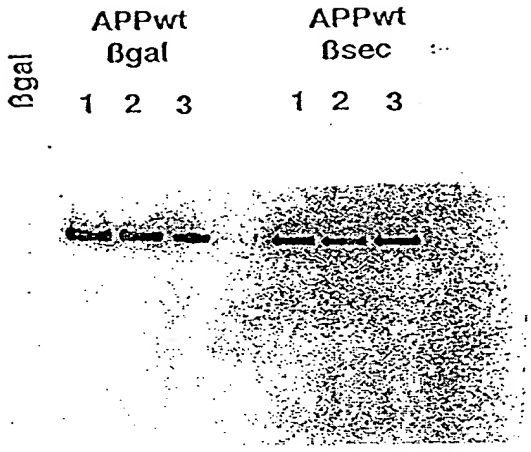


FIG. 17A

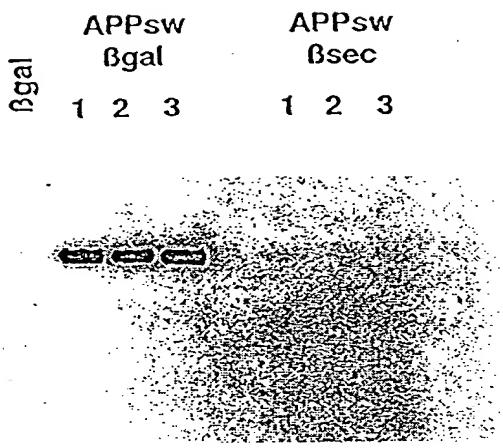


FIG. 17B

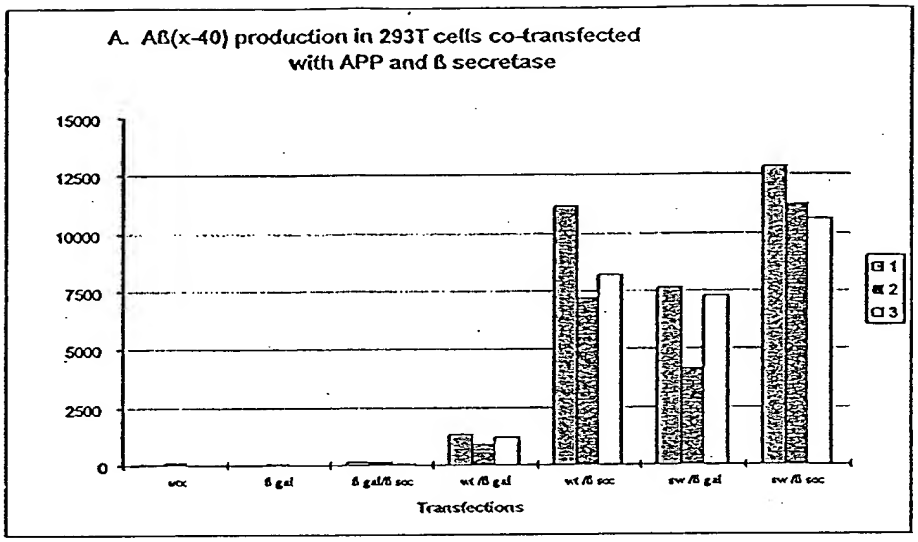

A. Aß(x-40) production in 293T cells co-transfected with APP and ß secretase
15000
12500
10000
7500
5000
2500
0
Transfections
1
2
3

FIG. 18

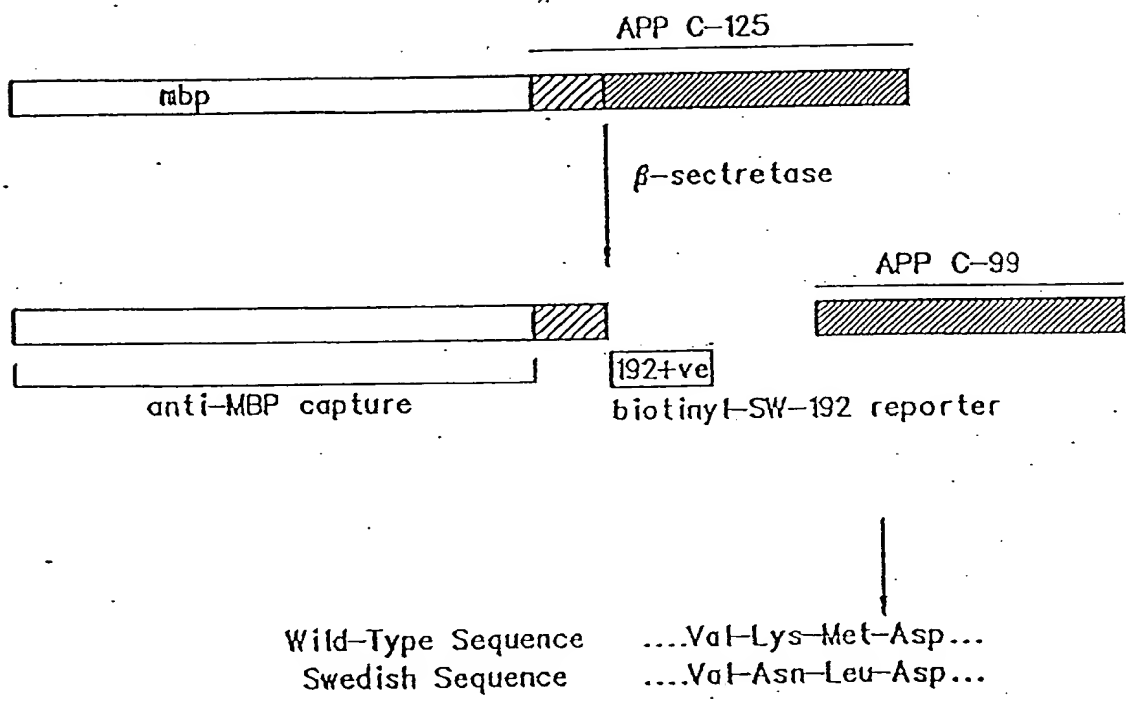

APP C–125
mbp
β–sectretase
APP C–99
192+ve
anti–MBP capture
biotinyl–SW–192 reporter
Wild–Type Sequence ....Val–Lys–Met–Asp...
Swedish Sequence ....Val–Asn–Leu–Asp...

FIG. 19

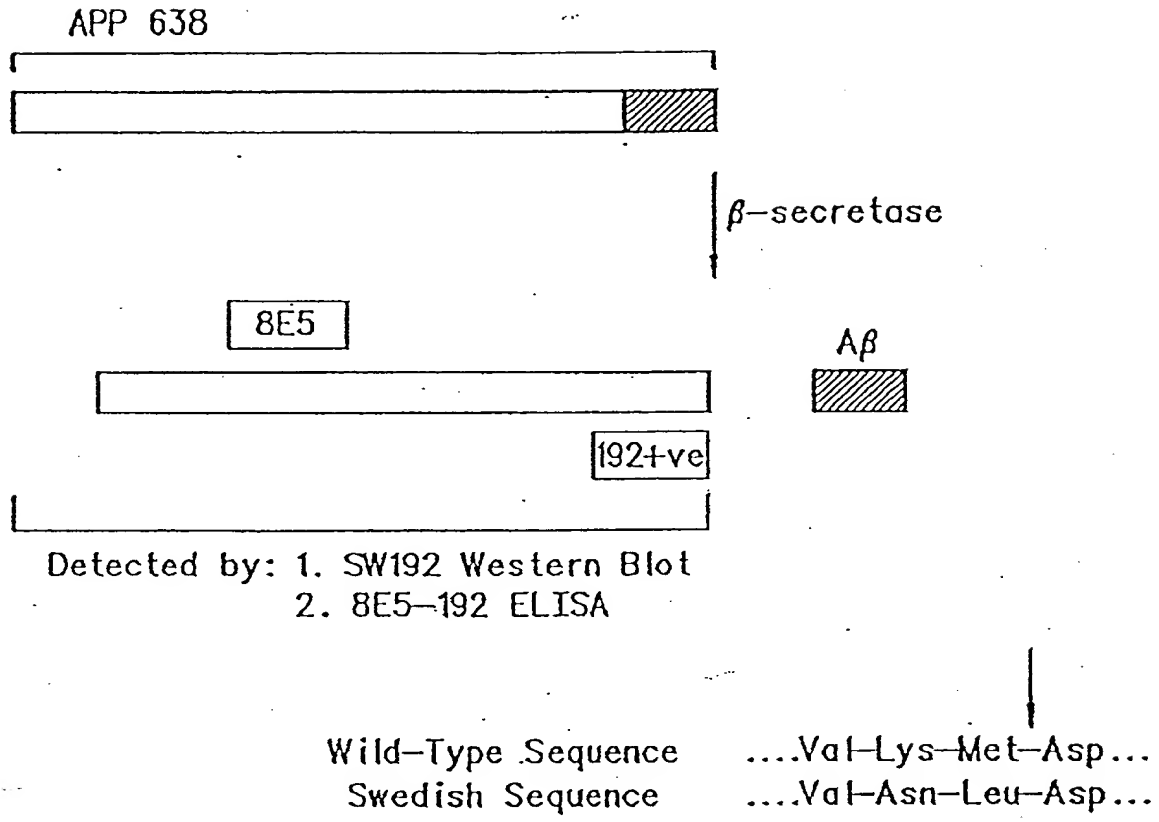

APP 638
β–secretase
8E5
Aβ
192+ve
Detected by: 1. SW192 Western Blot
2. 8E5–192 ELISA
Wild–Type Sequence ....Val–Lys–Met–Asp...
Swedish Sequence ....Val–Asn–Leu–Asp...

FIG. 20

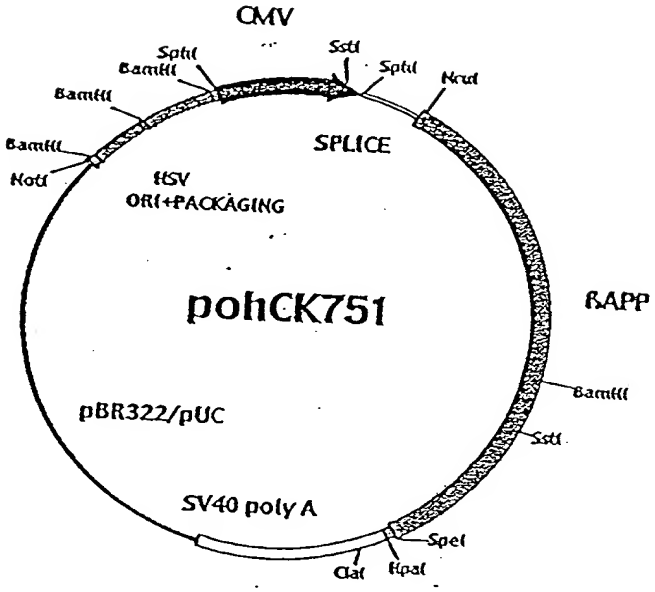

CMV
SplI
BamHI
SstI
SplI
NruI
BamHI
BamHI
SPLICE
BamHI
NotI
HSV
ORI+PACKAGING
pohCK751
BAPP
BamHI
pBR322/pUC
SstI
SV40 poly A
SpeI
ClaI
KpnI

FIG. 21